REMARKS

Claims 1-2, 4-17, 19-25 are currently pending in the application. Claims 3 and 18 are canceled. Claims 1 and 14 are amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1-25 are rejected as alleged being indefinite. The claims recite the step "generating duplexes in said amplified products," e.g., in independent claims 1 and 14. The Office Action states that the claims are confusing because the amplified products created are already in duplex form, thus, "it cannot be understood how one is to 'generate duplexes in said amplified products' when said products already are duplexes."

Without acquiescing to the rejections, Applicants have amended claims 1 and 14 to recite the duplex generation step as "denaturing said amplified products and re-generating duplexes in said reaction mixture." Applicants submit this can be done by denaturing the amplified products and allow them to re-anneal with each other or any other nucleic acid molecules present in the same reaction mixture, which may generate heteroduplex for detection. When a PCR amplification is carried out to generate amplified products according to one embodiment of the present invention as claimed in claims 1-25, the denaturing and re-annealing of nucleic acids occur during the amplification process, which consists a number of temperature cycles designed for denaturing of template nucleic acids and annealing of the primers to the denatured templates. The amendments find support throughout the specification, e.g., page 14, lines 8-13; page 50, lines 8-18; and page 59, line 26 to page 60, line 9. No new matter is added.

Rejections Under 35 U.S.C. §102 (b)

The Office Action states claims 1-2, 4, 7-14, 16-17, 19 and 21-25 are rejected as alleged for lack of novelty over Watnick et al. (1997) or Turco et al. (1995). The Office Action states that each reference teaches a method of amplifying a nucleic acid using two primers which bind to SEQ ID NO: 1 or 2, subjecting amplification products to heteroduplex analysis and detecting any heteroduplex as an indication of the presence of a mutation.

Applicants respectfully disagree.

First, Applicants submit that the Office Action failed to show that Watnick et al. (1997) or Turco et al. (1995) teaches a sequence identical to SEQ ID NO: 1 or 2.

Second, without acquiescing to the rejections, Applicants have amended claims 1 and 14 to recite "said first or second nucleic acid comprises a sequence selected from the group consisting of SEQ ID NOs. 3-49." Neither Watnick et al. nor Turco et al. teaches a method using a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 3-49. Therefore, Watnick et al. or Turco et al. does not anticipate the present invention as claimed in the amended claims 1 and 14, or their dependent claims.

Applicants respectfully request the reconsideration and withdrawal of the 102(b) rejections over claims 1, 2, 4, 7-14, 16-17, 19, and 21-25.

Rejections Under 35 U.S.C. §102 (e)

Claims 1, 2, 4, 6-17, 19, and 21-25 are rejected as alleged for lack of novelty over Germino et al. (US 2003/0008288). The Office Action states that Germino et al. teaches the claimed methods.

Applicants respectfully disagree.

First, Applicants submit that the Office Action failed to show that Germino et al. teaches a sequence identical to SEQ ID NO: 1 or 2.

Second, as stated above and without acquiescing to the rejections, Applicants have amended claims 1 and 14 to recite "said first or second nucleic acid comprises a sequence selected from the group consisting of SEQ ID NOs. 3-49." Germino et al. does not teaches a method using nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 3-49. Therefore, Germino et al. does not anticipate the present invention as claimed in the amended claims 1 and 14, or their dependent claims.

Applicants respectfully request the reconsideration and withdrawal of the 102(e) rejections over claims 1, 2, 4, 6-17, 19, and 21-25.

Rejections Under 35 U.S.C. §103(a)

Claims 6 and 15 are rejected under 35 U.S.C. §103(a) as alleged being obvious over either Watnick et al. or Turco et al. in view of Liu et al. The Office Action states that although neither Watnick et al. nor Turco et al. teaches the detection of heretoduplex by the technique of DHPLC, Liu et al teaches that the technique of DHPLC is an advantage means of detecting mutations and polymorphisms. The Office Action concludes that one of ordinary skill in the art would have been motivated to modify the method of Watnick et al. or Turco et al. by using DHPLC as taught in Liu et al.

Applicants respectfully disagree.

First, Applicants submit that the difficulty of developing a DNA-based testing method for ADPKD has long been recognized in the art. But there were many technical obstacles that prevented such development prior to the filing date of the present application. For example, the instant specification states:

> One serious obstacle for developing a DNA-based testing method for ADPKD is that sequences related to the PKD transcript, for example, PKD-1, are duplicated at least three times on chromosome 16 proximal to the PKD-1 locus, forming PKD-1 homologues. Another obstacle is that the PKD-1 genomic interval also contains repeat elements that are present in other genomic regions. In addition, the sequences of PKD genes are extremely GC rich and a large number (15,816 bp) of nucleotides need to be analyzed for a thorough evaluation. (page 2, lines 22-27).

Applicants submit that there has been no publications teaching the method of mutation analysis of SEQ ID NO. 1 or 2 since Liu et al. was published in 1998, 4 years prior to the filing of the present application. Therefore, Applicants of the present invention solved a long felt but unsolved need in the art.

Second, without acquiescing to the rejections, Applicants have amended claims 1 and 14 to recite "said first or second nucleic acid comprises a sequence selected from the group

consisting of SEQ ID NOs. 3-49." As discussed above, neither Watnick et al. nor Turco et al. teaches or suggests a method using a nucleic acid comprising a specific sequence selected from the group consisting of SEQ ID NOs. 3-49. Liu et al. does not teach or suggest such a method either. The combination of Watnick et al. or Turco et al. in view of Liu et al. does not teach or suggest the claimed method in claims 1 and 14. Claims 6 and 15 depend from claims 1 and 14 respectively, therefore, the combination of Watnick et al. or Turco et al. in view of Liu et al. does not teach or suggest the claimed method in claims 6 and 15.

Applicants respectfully request the reconsideration and withdrawal of the 103(a) rejections over claims 6 and 15.

Allowable Subject Matter

The Office Action states the subject matter in claims 3, 5, 18, and 20 are allowable. Applicants submit that claims 1 and 14 have been amended to encompass the allowable subject matter of claims 3, 5, 18, and 20. Original claims 3 and 18 are cancelled in view of the above amendments. As discussed, the amendments are supported in the specification and in claims 3 and 18 as originally filed. No new matter is added.

Conclusion

Applicant submits that all pending claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

Date: October 7, 2004

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